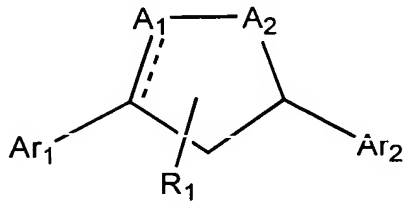
Amendments to the Claims

Please cancel Claims 22-29 and 45-56. The Claim Listing below will replace all prior versions of the claims in the application:

Claim Listing

1. (Original) A compound of Formula (I) or a pharmaceutically acceptable salt thereof:



(I)

wherein:

Ar_1 and Ar_2 are independently a monocyclic six-member optionally substituted heteroaryl group;

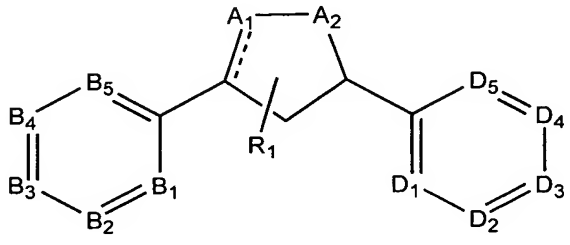
A_1 is =N– or –NR^a– and A_2 is O or S;

R^a is H or C1-C6 alkyl;

R_1 is selected from -H, C1-C6 alkyl, phenyl, C1-C6 haloalkyl, halogen, -OH, -OR^b, C1-C6 hydroxyalkyl, C1-C6 alkoxyalkyl, -O(C1-C6 haloalkyl), -SH, -SR^b, -NO_2, -CN, -$NR^bCO_2R^b$, -$NR^bC(O)R^b$, -CO_2R^b, -$C(O)R^b$, -$C(O)N(R^b)_2$, -$OC(O)R^b$ and -NR^bR^b; and

each R^b is H or a C1-C6 alkyl group.

2. (Original) The compound of Claim 1 represented by Formula (II):



(II)

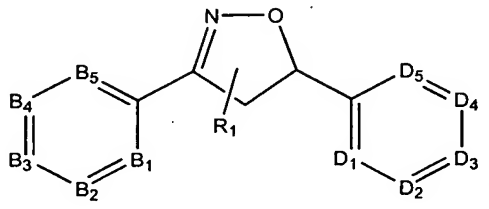
wherein:

B_1 through B_5 and D_1 through D_5 are independently N or CR^c, provided that from one to three of B_1 through B_5 and from one to three of D_1 through D_5 are N;

each R^c is independently -H, C1-C6 alkyl, halogen, C1-C6 haloalkyl, $-R^o$, -OH, $-OR^o$, -O(C1-C6 haloalkyl), -SH, $-SR^o$, $-NO_2$, -CN, $-NHCO_2R^o$, -NHC(O)H, $-NHC(O)R^o$, $-CO_2H$, $-CO_2R^o$, -C(O)H, $-C(O)R^o$, $-C(O)NHR^o$, $-OC(O)R^o$, $-S(O)_2R^o$, $-SO_2NH_2$, $-S(O)R^o$, $-NHSO_2R^o$, $-N(R^o)_2$, $-NR^oC(O)R^o$, or $-C(O)N(R^o)_2$ or a C1-C6 alkyl group substituted with R^o, -OH, $-OR^o$, -SH, $-SR^o$, $-NO_2$, -CN, $-NHCO_2R^o$, -NHC(O)H, $-NHC(O)R^o$, $-CO_2H$, $-CO_2R^o$, -C(O)H, $-C(O)R^o$, $-C(O)NHR^o$, $-OC(O)R^o$, $-S(O)_2R^o$, $-SO_2NH_2$, $-S(O)R^o$, $-NHSO_2R^o$; and

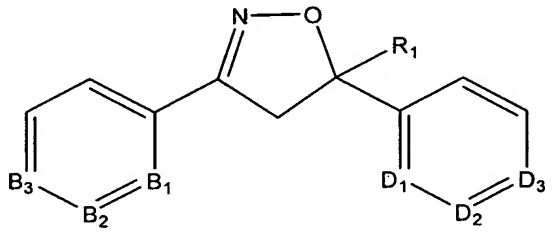
R^o is independently, C1-C6 alkyl, aryl or heteroaryl group and wherein the aryl or heteroaryl group represented by R^o is optionally substituted with one or more halogen, methyl or methoxy groups.

3. (Original) The compound of Claim 2 wherein the compound is represented by Formula (III):



(III).

4. (Original) The compound of Claim 3 wherein the compound is represented by Formula (IV):



(IV)

wherein one of B_1 through B_3 and one of D_1 through D_3 are N.

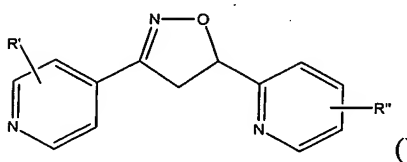
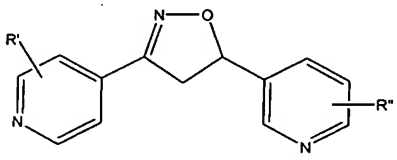
5. (Original) The compound of Claim 4 wherein R_1 is -H or a C1-C3 alkyl optionally substituted with a halogen or a hydroxyl.

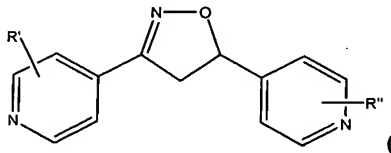
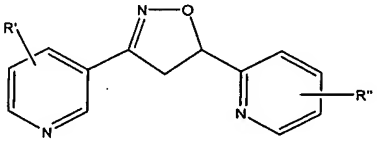
6. (Original) The compound of Claim 5 wherein

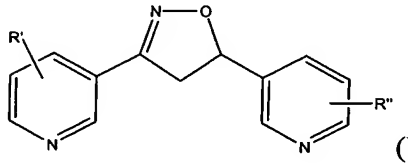
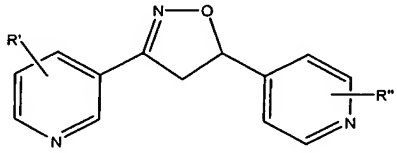
R^c is -H, halogen, $-NO_2$, -CN, C1-C3 alkyl, C1-C3 haloalkyl, C1-C3 hydroxyalkyl, C1-C3 alkoxyalkyl, $-N(R^d)_2$, $-NR^dC(O)R^d$, or $-C(O)N(R^d)_2$; and

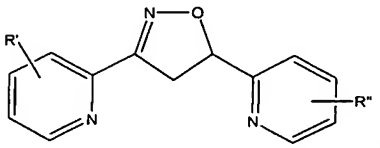
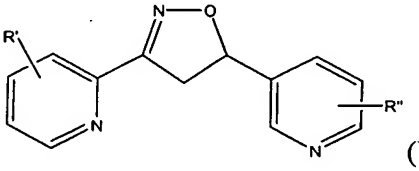
each R^d is H or a C1-C3 alkyl group.

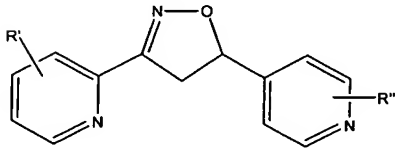
7. (Original) The compound of Claim 6 selected from the group consisting of:


(V a);

(V b);


(V c);

(V d);


(V e);

(V f);

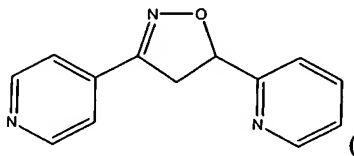

(V g);

(V h); and

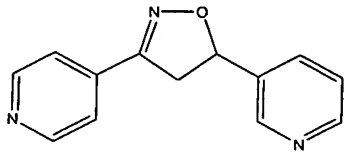

(V i).

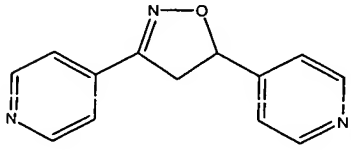
wherein:

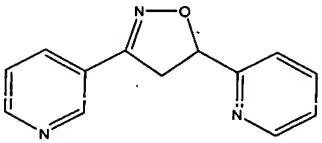
R' and R'' are independently -H, halogen, $-NO_2$, -CN, C1-C3 alkyl, C1-C3 haloalkyl, C1-C3 hydroxyalkyl, C1-C3 alkoxyalkyl, $-N(R^d)_2$, $-NR^dC(O)R^d$, or $-C(O)N(R^d)_2$.

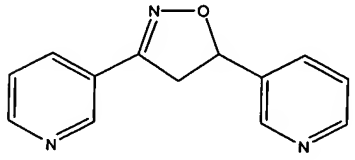
8. (Original) The compound of Claim 7 selected from the group consisting of:

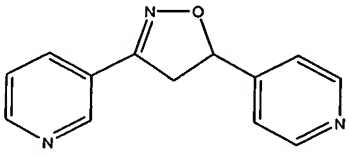
 (VI a);

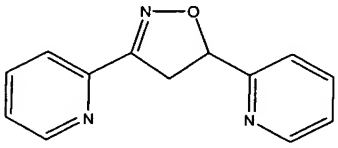
 (VI b);

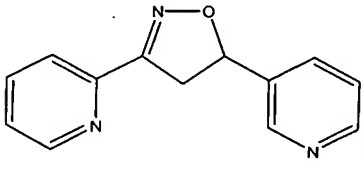
 (VIc);

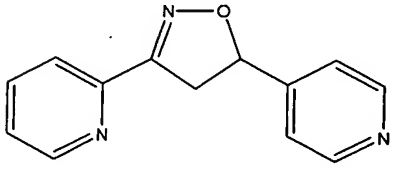
 (VI d);

 (VII e);

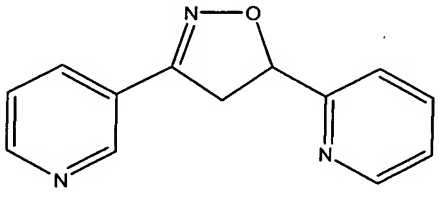
 (VI f);

 (VI g);

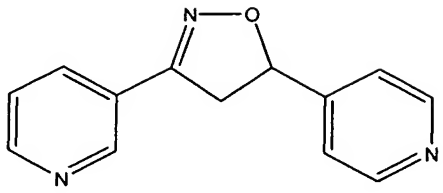
 (VI h); and

 (VI i).

9. (Original) The compound of Claim 8 represented by Formula (VId):

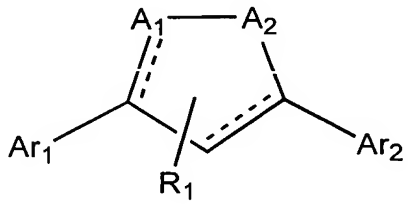
 (VId).

10. (Original) The compound of Claim 8 represented by Formula (VIf):



(VIf).

11. (Original) A pharmaceutical composition comprising a pharmaceutically acceptable carrier or diluent and a compound represented by Formula (I a) or a pharmaceutically acceptable salt thereof:



(I a)

wherein:

Ar_1 and Ar_2 are independently a monocyclic six-member optionally substituted heteroaryl group;

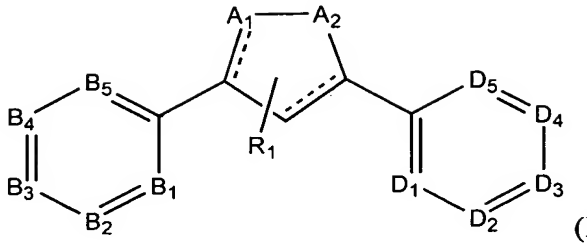
A_1 is =N– or –NR^a– and A_2 is O or S;

R^a is H or C1-C6 alkyl;

R_1 is selected from -H, C1-C6 alkyl, phenyl, C1-C6 haloalkyl, halogen, -OH, -OR^b, C1-C6 hydroxyalkyl, C1-C6 alkoxyalkyl, -O(C1-C6 haloalkyl), -SH, -SR^b, -NO_2, -CN, -$NR^bCO_2R^b$, -$NR^bC(O)R^b$, -CO_2R^b, -$C(O)R^b$, -$C(O)N(R^b)_2$, -$OC(O)R^b$ and -NR^bR^b; and

each R^b is H or a C1-C6 alkyl group.

12. (Original) The composition of Claim 11 wherein the compound is represented by Formula (II a):



(II a)

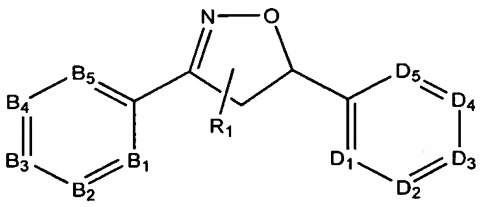
wherein:

B_1 through B_5 and D_1 through D_5 are independently N or CR^c, provided that from one to three of B_1 through B_5 and from one to three of D_1 through D_5 are N;

each R^c is independently -H, C1-C6 alkyl, halogen, C1-C6 haloalkyl, $-R^o$, -OH, $-OR^o$, -O(C1-C6 haloalkyl), -SH, $-SR^o$, $-NO_2$, -CN, $-NHCO_2R^o$, -NHC(O)H, $-NHC(O)R^o$, $-CO_2H$, $-CO_2R^o$, -C(O)H, $-C(O)R^o$, $-C(O)NHR^o$, $-OC(O)R^o$, $-S(O)_2R^o$, $-SO_2NH_2$, $-S(O)R^o$, $-NHSO_2R^o$, $-N(R^o)_2$, $-NR^oC(O)R^o$, $-C(O)N(R^o)_2$ or a C1-C6 alkyl group substituted with R^o, -OH, $-OR^o$, -SH, $-SR^o$, $-NO_2$, -CN, $-NHCO_2R^o$, -NHC(O)H, $-NHC(O)R^o$, $-CO_2H$, $-CO_2R^o$, -C(O)H, $-C(O)R^o$, $-C(O)NHR^o$, $-OC(O)R^o$, $-S(O)_2R^o$, $-SO_2NH_2$, $-S(O)R^o$ or $-NHSO_2R^o$;

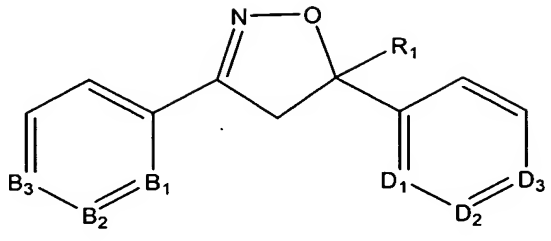
R^o is independently C1-C6 alkyl, aryl or heteroaryl group and wherein the aryl or heteroaryl group represented by R^o is optionally substituted with one or more halogen, methyl or methoxy groups.

13. (Original) The composition of Claim 12 wherein the compound is represented by Formula (III):



(III)

14. (Original) The composition of Claim 13 wherein the compound is represented by Formula (IV):



(IV)

wherein one of B_1 through B_3 and one of D_1 through D_3 are N.

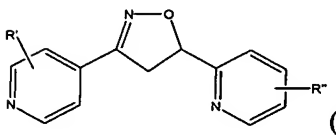
15. (Original) The composition of Claim 14 wherein R_1 is -H or a C1-C3 alkyl optionally substituted with a halogen or a hydroxyl.

16. (Original) The composition of Claim 15 wherein

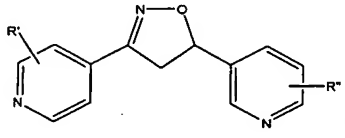
R^c is -H, halogen, $-NO_2$, -CN, C1-C3 alkyl, C1-C3 haloalkyl, C1-C3 hydroxyalkyl or C1-C3 alkoxyalkyl, $-N(R^d)_2$, $-NR^dC(O)R^d$, or $-C(O)N(R^d)_2$; and

each R^d is H or a C1-C3 alkyl group.

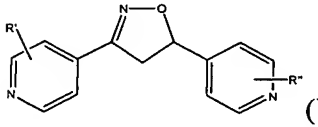
17. (Original) The composition of Claim 16 wherein the compound is selected from the group consisting of:



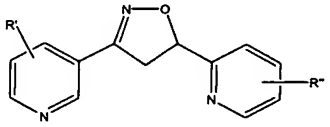
(V a);



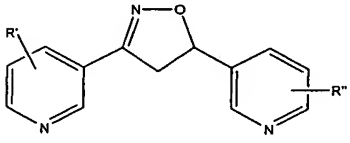
(V b);



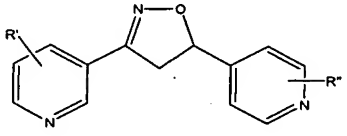
(V c);



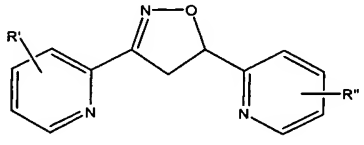
(V d);



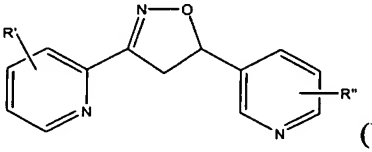
(V e);



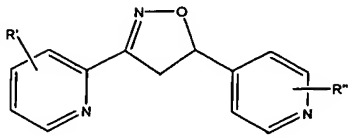
(V f);



(V g);



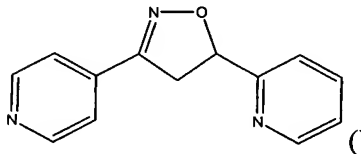
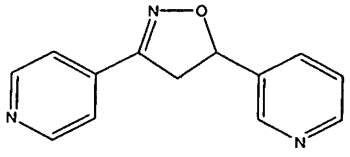
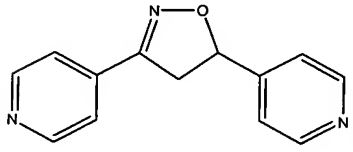
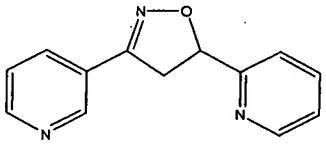
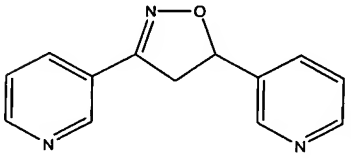
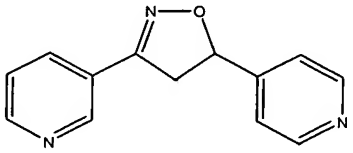
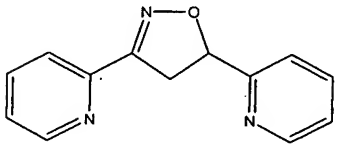
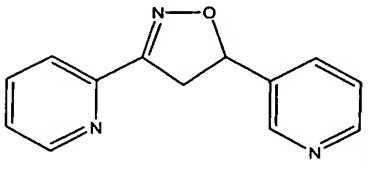
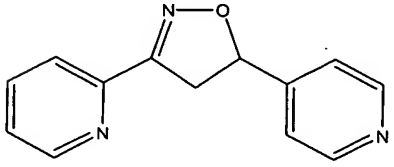
(V h); and


(V i),

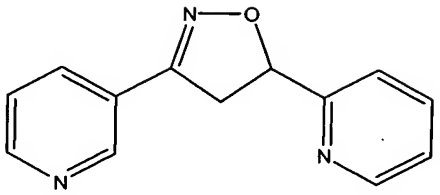
wherein

R' and R'' are independently -H, halogen, $-NO_2$, -CN, C1-C3 alkyl, C1-C3 haloalkyl, C1-C3 hydroxyalkyl, C1-C3 alkoxyalkyl, $-N(R^d)_2$, $-NR^dC(O)R^d$, or $-C(O)N(R^d)_2$.

18. (Original) The composition of Claim 17 wherein the compound is selected from the group consisting of:

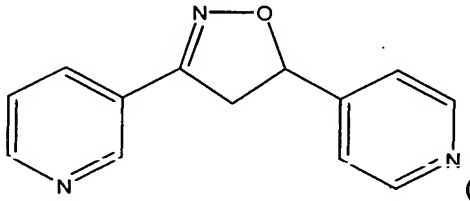

(VI a);

(VI b);

(VI c);

(VI d);

(VI e);

(VI f);

(VI g);

(VI h); and

(VI i).

19. (Original) The composition of Claim 18 wherein the compound is represented by Formula (VId):



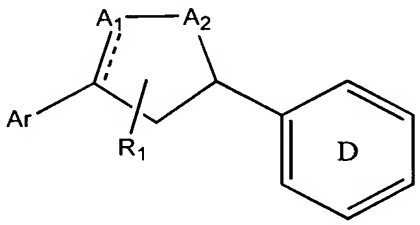
(VId).

20. (Original) The composition of Claim 18 wherein the compound is represented by Formula (VIf):



(VIf).

21. (Original) A pharmaceutical composition comprising a pharmaceutically acceptable carrier or diluent and a compound represented by Formula (VII) or a pharmaceutically acceptable salt thereof:



(VII)

wherein:

Ar is an optionally substituted, monocyclic, six-member heteroaryl;

A_1 is =N– or –NR^a– and A_2 is O or S;

R_1 is -H, C1-C6 alkyl, phenyl, C1-C6 haloalkyl, halogen, -OH, -OR^b, C1-C6 hydroxyalkyl, C1-C6 alkoxyalkyl, -O(C1-C6 haloalkyl), -SH, -SR^b, -NO_2, -CN, -NR^bCO_2 R^b, -$NR^bC(O)$ R^b, -CO_2R^b, -$C(O)R^b$, -$C(O)N(R^b)_2$, -$OC(O)R^b$ or -NR^bR^b;

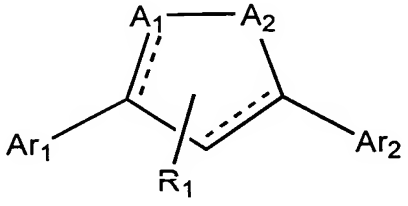
each R^a is -H or C1-C6 alkyl;

each R^b is -H or a C1-C6 alkyl group; and

ring **D** is optionally substituted with zero, one or more substituents other than amide and is not an alkylphenol.

22-29. (Cancelled)

30. (Original) A method of treating a subject with an inflammatory cytokine mediated disorder comprising administering to the subject a therapeutically effective amount of a compound represented by Formula (I) or a pharmaceutically acceptable salt thereof:



(I a)

wherein:

Ar_1 and Ar_2 are independently monocyclic six-member optionally substituted heteroaryl groups;

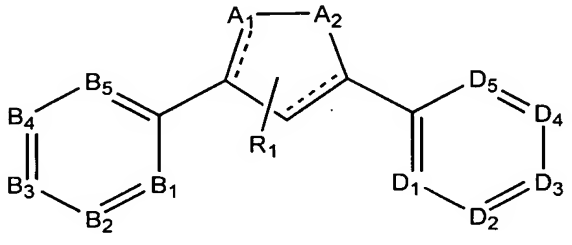
A_1 is =N– or –NR^a– and A_2 is O or S;

R^a is -H or C1-C6 alkyl;

R_1 is y selected from -H, C1-C6 alkyl, phenyl, C1-C6 haloalkyl, halogen, -OH, -OR^b, C1-C6 hydroxyalkyl, C1-C6 alkoxyalkyl, -O(C1-C6 haloalkyl), -SH, -SR^b, -NO_2, -CN, -NR^bCO_2 R^b, -$NR^bC(O)$ R^b, -CO_2R^b, -$C(O)R^b$, -$C(O)N(R^b)_2$, -$OC(O)R^b$ and -NR^bR^b; and

R^b is -H or a C1-C6 alkyl group.

31. (Original) The method of Claim 30, wherein the compound is represented by Formula (II a):



(II a)

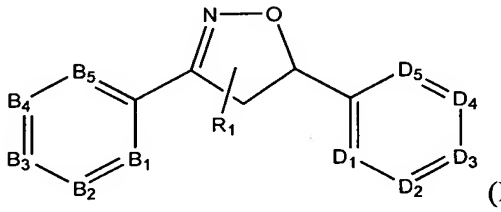
wherein:

B_1 through B_5 and D_1 through D_5 are independently N or CR^c, provided that from one to three of B_1 through B_5 and from one to three of D_1 through D_5 are N;

each R^c is independently -H, C1-C6 alkyl, halogen, C1-C6 haloalkyl, $-R^o$, -OH, $-OR^o$, -O(C1-C6 haloalkyl), -SH, $-SR^o$, $-NO_2$, -CN, $-NHCO_2R^o$, -NHC(O)H, $-NHC(O)R^o$, $-CO_2H$, $-CO_2R^o$, -C(O)H, $-C(O)R^o$, $-C(O)NHR^o$, $-OC(O)R^o$, $-S(O)_2R^o$, $-SO_2NH_2$, $-S(O)R^o$, $-NHSO_2R^o$, $-N(R^o)_2$, $-NR^oC(O)R^o$, $-C(O)N(R^o)_2$ or a C1-C6 alkyl group substituted with R^o, -H, $-OR^o$, -SH, $-SR^o$, $-NO_2$, -CN, $-NHCO_2R^o$, -NHC(O)H, $-NHC(O)R^o$, $-CO_2H$, $-CO_2R^o$, -C(O)H, $-C(O)R^o$, $-C(O)NHR^o$, $-OC(O)R^o$, $-S(O)_2R^o$, $-SO_2NH_2$, $-S(O)R^o$ or $-NHSO_2R^o$; and

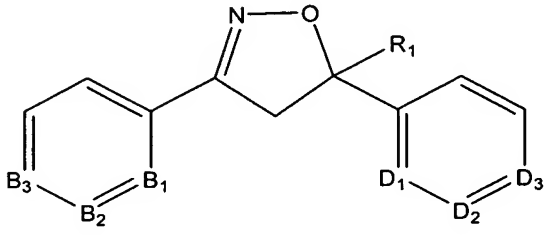
R^o is independently C1-C6 alkyl, aryl or heteroaryl group and wherein the aryl or heteroaryl group represented by R^o is optionally substituted with one or more halogen, methyl or methoxy groups.

32. (Original) The method of Claim 31 wherein the compound is represented by Formula (III):



(III).

33. (Original) The method of Claim 32 wherein the compound is represented by Formula (IV):



(IV)

wherein one of B_1 through B_3 and one of D_1 through D_3 are N.

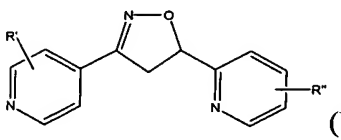
34. (Original) The method of Claim 33 wherein R_1 is -H or a C1-C3 alkyl, optionally substituted with a halogen or a hydroxyl.

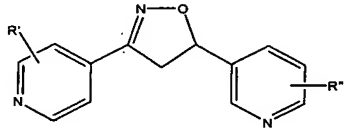
35. (Original) The method of Claim 34 wherein

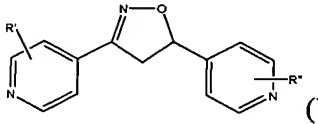
R^c is -H, halogen, $-NO_2$, -CN, C1-C3 alkyl, C1-C3 haloalkyl, C1-C3 hydroxyalkyl, C1-C3 alkoxyalkyl, $-N(R^d)_2$, $-NR^dC(O)R^d$, $-C(O)N(R^d)_2$; and

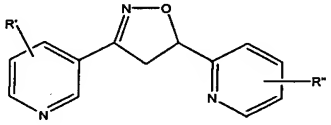
each R^d is H or a C1-C3 alkyl group.

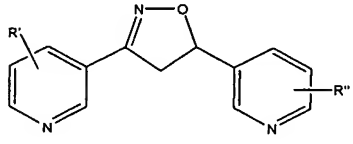
36. (Original) The method of Claim 35 wherein the compound is selected from the group consisting of:

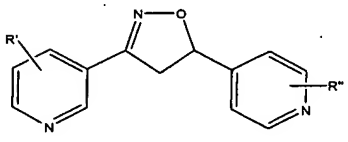

(V a);

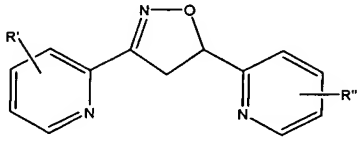

(V b);

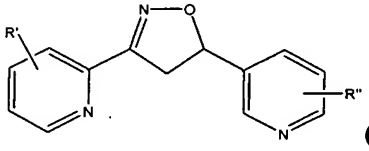

(V c);

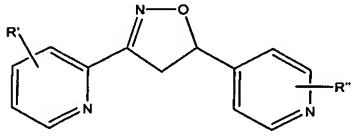

(V d);


(V e);


(V f);


(V g);

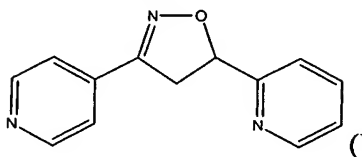
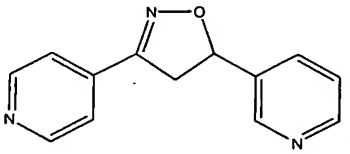
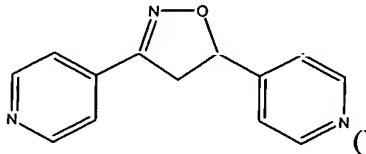
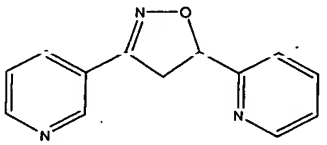
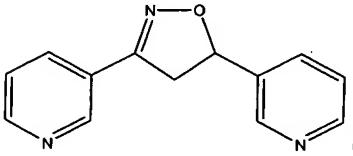
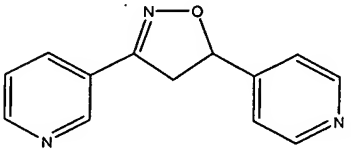
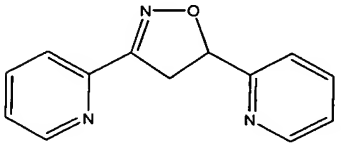
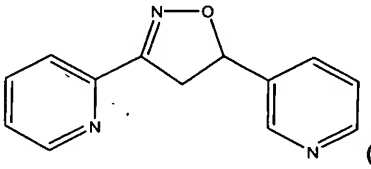
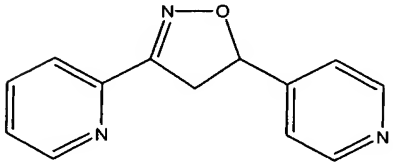

(V h); and


(V i),

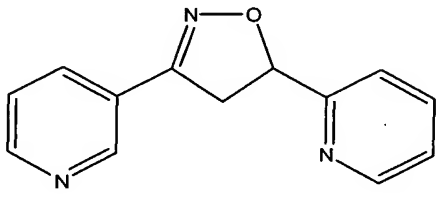
wherein

R' and R'' are independently -H, halogen, $-NO_2$, -CN, C1-C3 alkyl, C1-C3 haloalkyl, C1-C3 hydroxyalkyl, C1-C3 alkoxyalkyl, $-N(R^d)_2$, $-NR^dC(O)R^d$, $-C(O)N(R^d)_2$.

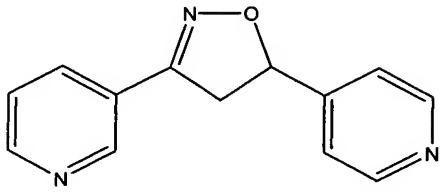
37. (Original) The method of Claim 36 wherein the compound is selected from the group consisting of:


(VI a);

(VI b);

(VI c);

(VI d);

(VI e);

(VI f);

(VI g);

(VI h); and

(VI i).

38. (Original) The method of Claim 37 wherein the compound is represented by Formula (VId):


(VId).

39. (Original) The method of Claim 37 wherein the compound is represented by Formula (VIf):



(VIf).

40. (Original) The method of Claim 30 wherein the inflammatory cytokine is TNF-α or HMGB-1.

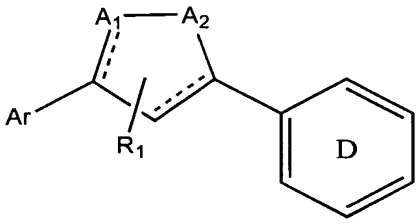
41. (Original) The method of Claim 40 wherein the disorder is selected from the group consisting of appendicitis, peptic, gastric or duodenal ulcers, peritonitis, pancreatitis, ulcerative, pseudomembranous, acute or ischemic colitis, diverticulitis, epiglottitis, achalasia, cholangitis, cholecystitis, hepatitis, Crohn's disease, enteritis, Whipple's disease, asthma, allergy, anaphylactic shock, immune complex disease, organ ischemia, reperfusion injury, organ necrosis, hay fever, sepsis, septicemia, endotoxic shock, cachexia, hyperpyrexia, eosinophilic granuloma, granulomatosis, sarcoidosis, septic abortion, epididymitis, vaginitis, prostatitis, urethritis, bronchitis, emphysema, rhinitis, cystic fibrosis, pneumonitis, pneumoultramicroscopic silicovolcanoconiosis, alvealitis, bronchiolitis, pharyngitis, pleurisy, sinusitis, influenza, respiratory syncytial virus infection, herpes infection, HIV infection, hepatitis B virus infection, hepatitis C virus infection, disseminated bacteremia, Dengue fever, candidiasis, malaria, filariasis, amebiasis, hydatid cysts, burns, dermatitis, dermatomyositis, sunburn, urticaria, warts, wheals, vasulitis, angiitis, endocarditis, arteritis, atherosclerosis, thrombophlebitis, pericarditis, myocarditis, myocardial ischemia, periarteritis nodosa, rheumatic fever, Alzheimer's disease, coeliac disease, congestive heart failure, adult respiratory distress syndrome, meningitis, encephalitis, multiple sclerosis, cerebral infarction, cerebral embolism, Guillame-Barre syndrome, neuritis, neuralgia, spinal cord injury, paralysis, uveitis, arthritides, arthralgias, osteomyelitis, fasciitis, Paget's disease, gout, periodontal disease, rheumatoid arthritis, synovitis, myasthenia gravis, thryoiditis, systemic lupus erythematosus, Goodpasture's syndrome, Behcets's syndrome, allograft rejection, graft-versus-host disease, Type I diabetes, ankylosing

spondylitis, Berger's disease, Type I diabetes, ankylosing spondylitis, Retier's syndrome, or Hodgkins disease. In more preferred embodiments, the condition is appendicitis, peptic, gastric or duodenal ulcers, peritonitis, pancreatitis, ulcerative, pseudomembranous, acute or ischemic colitis, hepatitis, Crohn's disease, asthma, allergy, anaphylactic shock, organ ischemia, reperfusion injury, organ necrosis, hay fever, sepsis, septicemia, endotoxic shock, cachexia, septic abortion, disseminated bacteremia, burns, Alzheimer's disease, coeliac disease, congestive heart failure, adult respiratory distress syndrome, cerebral infarction, cerebral embolism, spinal cord injury, paralysis, allograft rejection and graft-versus-host disease.

42. (Original) The method of Claim 41 wherein the disorder is selected from the group consisting of peritonitis, pancreatitis, ulcerative colitis, Crohn's disease, asthma, organ ischemia, reperfusion ischemia, sepsis, cachexia, burns, myocardial ischemia, adult respiratory distress syndrome, multiple sclerosis, rheumatoid arthritis, systemic lupus erythematous, chronic obstructive pulmonary disease, psoriasis, Behcet's syndrome, allograft rejection and graft-versus-host disease.

43. (Original) The method of Claim 42 wherein the disorder is sepsis.

44. (Original) A method of treating a subject with an inflammatory cytokine mediated disorder comprising administering to the subject a therapeutically effective amount of a compound represented by Formula (VIIa) or a pharmaceutically acceptable salt thereof:



(VIIa)

wherein

Ar is an optionally substituted, monocyclic, six-member heteroaryl;

A_1 is =N– or –NR^a– and A_2 is O or S;

R_1 is -H, C1-C6 alkyl, phenyl, C1-C6 haloalkyl, halogen, -OH, -OR^b, C1-C6 hydroxyalkyl, C1-C6 alkoxyalkyl, -O(C1-C6 haloalkyl), -SH, -SR^b, -NO_2, -CN, -NR^bCO_2 R^b, -$NR^bC(O)$ R^b, -CO_2R^b, -$C(O)R^b$, -$C(O)N(R^b)_2$, -$OC(O)R^b$ or -NR^bR^b;

each R^a is -H or C1-C6 alkyl group;

each R^b is -H or a C1-C6 alkyl group;

ring **D** is optionally substituted with zero, one or more substituents other than amide and is not an alkylphenol.

45-56. (Cancelled)